AMENDMENTS TO THE CLAIMS

The following is a complete listing of the claims submitted in this application, including the present status thereof and including any amendments made by this paper. Any claims canceled or withdrawn from consideration in this application have been canceled or withdrawn without prejudice or disclaimer of any subject matter therein, applicants specifically reserving the right to pursue any and all claims in continuing or divisional applications. By this paper, claims 115 and 127 have been amended. Claims 115, 116, 118, 120-121 and 126-131 remain under consideration in this application.

Listing of claims:

1-55(canceled).

56(withdrawn). A method of treatment of a chronic inflammatory disease in a patient, the method comprising the administration to the patient of a compound that selectively inhibits T_{ck} cells.

57(withdrawn). A method according to claim 56 wherein said compound is a nucleic acid molecule encoding a polypeptide which selectively inhibits T_{ck} cells.

58(withdrawn). A method according to claim 56 wherein said compound selectively inhibits T_{ck} cell-induced release of one or more pro-inflammatory cytokines from monocytes.

59(withdrawn). A method according to claim 58 wherein the cytokine is tumour necrosis factor-α.

60(withdrawn). A method according to any one of claims 56-59 wherein said compound selectively inhibits NF-κB.

61(withdrawn). A method according to any one of claim 56-59 wherein said compound selectively activates PI3 kinase.

62(withdrawn). A method according to claim 60 wherein the nucleic acid molecule encodes an NF-kB inhibitor, preferably IκBα.

63(withdrawn). A method according to claim 61 wherein the nucleic acid molecule encodes an NF-kB inhibitor, preferably IκBα.

64-66(canceled).

67(withdrawn). A method according to claim 66 wherein said method comprises the following steps:

(i) pre-incubating monocytes with a compound to be tested;

(ii) resuspending said pre-incubated monocytes in the absence of the test compound;

(iii) stimulating said resuspended monocytes by co-culturing with either T_{ck} cells or T_{tcr} cells; and

(iv) assaying for TNFα production by said stimulated monocytes.

68-70(canceled).

71(withdrawn). A method according to claim 64 wherein testing the compound for an ability to selectively inhibit T_{ck} cells or selectively inhibit T_{ck} cell-induced release of one or more pro-inflammatory cytokines from monocytes comprises determining whether the compound exhibits NF-κB inhibition.

72(withdrawn). A method according to claim 71 wherein NF-κB inhibition is constituted by a reduction in the binding of nuclear extracts, derived from monocytes exposed to the compound, to an NF-κB promoter DNA oligonucleotide.

73(withdrawn). A method according to claim 72 wherein a reduction in the binding of nuclear extracts, derived from monocytes exposed to the compound, to an NF-κB promoter DNA oligonucleotide is determined by an electrophoretic mobility shift assay (EMSA).

74(withdrawn). A method according to any one of claims 71-73 wherein NF-κB inhibition is deemed to exist if the binding of NF-κB to an NF-κB promoter DNA oligonucleotide is reduced to no more than 50%, a presumption being strengthened as that percentage approaches zero.

75(withdrawn). A method according to claim 71 wherein NF-κB inhibition is constituted by a reduction in expression of the NF-κB gene.

76(withdrawn). A method according to claim 75 wherein a reduction in the expression of the NF-κB gene is determined by a reporter gene assay.

77(withdrawn). A method according to claim 76 wherein the reporter gene assay comprises coupling a β-galactosidase gene to the NF-κB gene and determining a reduction in β-galactosidase activity.

78(withdrawn). A method according to claim 77 wherein β-galactosidase activity is reduced to no more that 50%.

79(withdrawn). A method according to claim 64 wherein testing the compound for an ability to selectively target T_{ck} cells or selectively inhibit T_{ck} cell-induced release of one or more pro-inflammatory cytokines from monocytes comprises determining whether the compound exhibits PI3 kinase activation.

80(withdrawn). A method according to claim 79 wherein PI3 kinase activation is constituted by an increase in PI3 kinase activity in monocytes exposed by the compound.

81(withdrawn). A method according to claim 80 wherein PI3 kinase activation is deemed to exist if there is an increase in PI3

kinase activity equivalent to a range from at least 50% of the increase induced by IL-10 stimulation (100 ng/ml for 2 minutes), to an amount greater than the increase induced by IL-10 stimulation.

82(withdrawn). A compound identified as having efficacy in the treatment of a chronic inflammatory disease by testing the compound for an ability to selectively inhibit T_{ck} cells or selectively inhibit T_{ck} cell-induced release of one or more pro-inflammatory cytokines from monocytes.

83(withdrawn). An antibody-like molecule having specificity for T_{ck} cells.

84(withdrawn). An antibody-like molecule according to claim 83 selected from the group of molecules consisting of Fab molecules, $F(ab')_2$ molecules, Fv molecules, disulphide-linked Fv molecules, single chain Fv (scFv) molecules and single domain antibodies (dAbs).

85(withdrawn). An antibody-like molecule according to claim 83 wherein said antibody-like molecule is humanized.

86(withdrawn). An antibody-like molecule according to claim 84 wherein said antibody-like molecule is humanized.

87(withdrawn). A method of making an antibody-like molecule having specificity for T_{ck} cells.

88(withdrawn). An isolated cell that expresses an antibody-like molecule having a specificity for T_{ck} cells.

89(withdrawn). An isolated cell according to claim 88 wherein the cell is a hybridoma cell.

90(withdrawn). A method for identifying an antibody-like molecule having specificity for T_{ck} cells comprising the following steps:

(i) providing a population of T_{ck} cells; and

(ii) using said T_{ck} cells to screen a library of antibody-like molecules.

91(withdrawn). A method according to claim 90 wherein the antibody-like molecule library is a phage display library.

92(withdrawn). A compound comprising a target cell specific portion and a directly or indirectly cytotoxic portion, wherein the target cell specific portion comprises an antibody-like molecule having a specificity for T_{ck} cells.

93(withdrawn). A compound according to claim 92 wherein the antibody-like molecule is selected from the group of molecules consisting of Fab molecules, $F(ab')_2$ molecules, Fv molecules, disulphide-linked Fv molecules, single chain Fv (scFv) molecules and single domain antibodies (dAbs).

94(withdrawn). A compound according to claim 93 wherein said antibody-like molecule is humanized.

95(withdrawn). A compound according to any one of claims 92-94 wherein the cytotoxic portion is a directly cytotoxic portion

selected from the group consisting of radionuclides, ricin, ribonuclease, deoxyribonuclease, and *Pseudomonas* exotoxin A.

96(withdrawn). A compound according to any one of claims 92-94 wherein the cytotoxic portion is indirectly cytotoxic.

97(withdrawn). A compound according to any one of claims 92-94 wherein the cytotoxic portion is capable of inducing apoptosis of the target cells.

98(withdrawn). A compound according to any one of claims 92-94 wherein the cytotoxic portion is an enzyme.

99(withdrawn). A compound according to claim 97 wherein the cytotoxic portion is an enzyme.

100(withdrawn). A compound according to any one of claims 92-94 wherein the target cell specific portion and the cytotoxic portion are fused.

101(withdrawn). A compound according to claim 100 wherein the target cell specific portion and the cytotoxic portion are separated by a linker sequence.

102(withdrawn). A compound according to any one of claims 92-94 having a nucleic acid molecule encoding.

103(withdrawn). A compound according claim 101 having a nucleic acid molecule encoding.

104(withdrawn). A compound according to any one of claims 92-94 wherein said nucleic acid molecule is included in a vector.

105(withdrawn). A compound according to claim 103 wherein said nucleic acid molecule is included in a vector.

106(withdrawn). A compound according to claim 104 wherein said vector is included in a host cell line.

107(withdrawn). A compound according to claim 105 wherein said vector is included in a host cell line.

108(withdrawn). A compound according to claim 82 for use in the treatment of a chronic inflammatory disease.

109(withdrawn). A preparation of T-cell enriched cells wherein the cells are from tissue from a site of inflammation in a patient suffering from a chronic inflammatory disease.

110(withdrawn). A preparation of cells according to claim 109 wherein the chronic inflammatory disease is rheumatoid arthritis.

111(withdrawn). A preparation of cells according to claim 109 wherein the tissue is from the synovium.

112(withdrawn). A preparation of cells according to claim 110 wherein the tissue is from the synovium.

113(withdrawn). A preparation of cells according to any one of claims 109-112 wherein the T-cell enriched cells are CD3+-enriched cells.

114(withdrawn). A preparation of cells according to any one of claims 109-112 wherein the T-cell enriched cells are non-adherent cells.

115(currently amended). A method of identifying a compound with efficacy in the treatment of chronic inflammatory disease by testing the compound for an ability to selectively inhibit the ability of cytokine stimulated T cells (T_{ck} cells) to induce pro-inflammatory cytokine release from a monocyte;

wherein said method comprises the following steps:

(i) pre-incubating T_{ck} cells with a compound to be tested;

(ii) optionally resuspending the T_{ck} cells in the absence of the test compound;

(iii) co-culturing the T_{ck} cells with monocytes; and

(iv) assaying for the production of pro-inflammatory cytokines by the monocytes;

wherein said T_{ck} cells are produced by incubating a population of T cells with one or more cytokines or are isolated from synovial tissue;

wherein said T_{ck} cells have not been contacted with an anti-CD3 antibody;

wherein said T_{ck} cells are fixed prior to said co-culturing with monocytes; and

wherein ~~an~~ the ability of a compound to selectively inhibit said T_{ck} cell-induced cytokine release when compared to cytokine release induced by contacting monocytes with another T cell

population indicates that the compound has efficacy in the treatment of chronic inflammatory disease.

116(previously presented). A method according to claim 115 wherein said compound is an antibody having specificity for T_{ck} cells.

117(canceled).

118(previously presented). A method according to claim 115 wherein said pro-inflammatory cytokine is TNFα.

119(withdrawn). A method according to claim 90 further comprising the steps of:

(iii) selecting one or more antibody-like molecule(s) from said library which selectively bind said T_{ck} cells;

(iv) pre-incubating a population of Tck cells with said antibody-like molecule(s);

(v) co-culturing said population of Tck cells with monocytes; and

(vi) assaying for TNFα produced by said monocytes.

120(previously presented). A method according to claim 115 wherein said T_{ck} cells are produced by incubating a population of T cells with one or more cytokines.

121(previously presented). A method according to claim 115 wherein said T_{ck} cells are isolated from synovial tissue.

122-123(canceled).

124(withdrawn). A method according to claim 115 comprising determining whether the compound exhibits NF-κB activation.

125(withdrawn). A method according to claim 115 comprising determining whether the compound exhibits PI3 kinase activation.

126(previously presented). A method according to claim 115 wherein said chronic inflammatory disease is rheumatoid arthritis.

127(currently amended). A method according to claim 115 wherein said method comprises the following steps:

(i) incubating separate cultures of T_{ck} cells and T cell receptor-stimulated T cells (T_{tcr} cells) with a compound to be tested either prior to fixation or during ~~or after~~ the activation of said T cells;

(ii) resuspending each of said T_{ck} and T_{tcr} cell cultures in the absence of the test compound;

(iii) coculturing each of said resuspended cultures with monocytes to allow stimulation of the monocytes; and

(iv) assaying for TNFα production by said monocytes;

wherein said T_{tcr} cells that have been activated by triggering of the T cell receptor for antigen; and

wherein the ability of a compound to selectively inhibit T_{ck} cell-induced production of TNFα by monocytes ~~to a greater extent than~~ when compared to the inhibition of T_{tcr} cell-induced production

of TNFα by monocytes indicates that the compound has efficacy in the treatment of chronic inflammatory disease.

128(previously presented). A method according to claim 127 wherein said T_{tcr} cells have been activated by contacting them with anti-CD3 antibodies.

129(previously presented). A method according to claim 115 wherein said T_{ck} cells are produced by incubating a population of T cells with IL-15.

130(previously presented). A method according to claim 115 wherein said T_{ck} cells are produced by incubating a population of T cells with IL-6, TNF and IL-2.

131(previously presented). A method according to claim 115 wherein said T_{ck} cells are produced by incubating a population of T cells with IL-6, TNF and IL-15.